

Organic compounds → BICYCLO(3.3.1)NONANES AND BICYCLO(3.3.1)NONENES
AND THEIR USE AS FLAVOUR OR FRAGRANCE INGREDIENT*

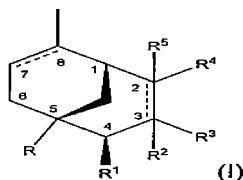
*Title changed by ISA

The present invention relates to substituted bicyclo[3.3.1]nonanes and
5 bicyclo[3.3.1]nonenes, having ambery, woody odour notes. This invention relates
furthermore to a method of their production and to flavour and fragrance compositions
comprising them.

10 In the fragrance industry there is always an ongoing demand for new compounds that
enhance or improve on odour notes, or impart new odour notes.

Surprisingly, we have found a novel class of compounds having much sought-after
ambery woody odour notes and which may be produced from readily-available cheap
and naturally available starting materials.

15 In a first aspect the invention refers to a compound of formula (I)



20 wherein
R is isopropyl or iso-propenyl;
R¹ is hydrogen, methyl or ethyl;
R² and R³ are independently hydrogen, methyl, or ethyl; or
R² and R³ taken together is ethylidene; or
25 R² and R³ taken together is a divalent radical (CH₂)₂ which forms cyclopropane together
with the carbon atom to which they are attached;
R⁴ and R⁵ are independently hydrogen, hydroxy, C₁ to C₃ alkoxy, e.g. methoxy, ethoxy,
or C₂ to C₃ acyloxy, e.g. acetoxy; or
R⁴ and R⁵ together with the carbon atom to which they are attached form a 1,3-
30 dioxolane ring or a 1,3-dioxane ring; or

R⁴ and R⁵ together with the carbon atom to which they are attached form a carbonyl group;

the bond between C2 and C3 is a single bond, or the dotted line together with the bond between C2 and C3 represents a double bond; and

5 the bond between C7 and C8 is a single bond, or the dotted line together with the bond between C7 and C8 represents a double bond.

The compounds according to the present invention contain several chiral centres and as such may exist as a mixture of stereoisomers, or they may be resolved as

10 isomerically pure forms. Resolving stereoisomers adds to the complexity of manufacture and purification of these compounds and so it is preferred to use the compounds as mixtures of their stereoisomers simply for economic reasons. However, if it is desired to prepare individual stereoisomers, this may be achieved according to methodology known in the art, e.g. preparative HPLC and GC or by stereoselective

15 syntheses.

Particular preferred compounds of formula (I) are 5-isopropenyl-4,8-dimethylbicyclo[3.3.1]non-7-en-2-one; 4-ethyl-5-isopropenyl-8-methylbicyclo[3.3.1]non-7-en-2-one; 5-isopropenyl-3,4,8-trimethylbicyclo[3.3.1]non-7-en-2-one; 5-isopropenyl-3,3,4,8-tetramethylbicyclo[3.3.1]non-7-en-2-one; 5-isopropenyl-8,8-dimethoxy-2,6-dimethylbicyclo[3.3.1]non-2-ene; 4,8-dimethyl-5-isopropenylspiro[bicyclo[3.3.1]nonane-2,2'-[1,3]dioxolane]; 5-isopropenyl-4,8-dimethylbicyclo[3.3.1]non-7-en-2-ol; 5-isopropenyl-2,4,8-trimethylbicyclo[3.3.1]non-7-en-2-ol; 5-isopropyl-4,8-dimethylbicyclo[3.3.1]nonan-2-one, 5-isopropenyl-8-methylbicyclo[3.3.1]non-7-en-2-one, 5-isopropenyl-3,4,8-trimethylbicyclo[3.3.1]non-7-en-2-one, and 4,8-dimethyl-5-isopropenyl-8-methoxy-bicyclo[3.3.1]non-7-ene.

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The compounds according to the present invention may be used alone or in combination with a base material. As used herein, the "base material" includes all known odourant molecules selected from the extensive range of natural and synthetic molecules currently available, such as essential oils, alcohols, aldehydes and ketones, ethers and acetals, esters and lactones, macrocycles and heterocycles, and/or in admixture with one or more ingredients or excipients conventionally used in conjunction with odourants in fragrance compositions, for example, carrier materials, and other

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35 auxiliary agents commonly used in the art.

The following list comprises examples of known odourant molecules, which may be combined with the compounds of the present invention:

- 5 – ethereal oils and extracts, e.g. tree moss absolute, basil oil, castoreum, costus root oil, myrtle oil, oak moss absolute, geranium oil, jasmin absolute, patchouli oil, rose oil, sandalwood oil, wormwood oil, lavender oil or ylang-ylang oil;
 - 10 – alcohols, e.g. citronellol, EbanolTM, eugenol, farnesol, geraniol, Super MuguetTM, linalool, phenylethyl alcohol, SandaloreTM, terpineol or TimberolTM.
 - 15 – aldehydes and ketones, e.g. α -amylcinnamaldehyd, GeorgywoodTM, hydroxycitronellal, Iso E Super[®], Isoraldeine[®], Hedione[®], maltol, methyl cedryl ketone, methylionone or vanillin;
 - 20 – ether and acetals, e.g. AmbroxTM, geranyl methyl ether, rose oxide or SpirambreneTM.
 - 25 – esters and lactones, e.g. benzyl acetate, cedryl acetate, γ -decalactone, Helvetolide[®], γ -undecalactone or vetivenyl acetate.
 - 30 – macrocycles, e.g. ambrettolide, ethylene brassylate or Exaltolide[®].
 - 35 – heterocycles, e.g. isobutylcholine.
- 25 The compounds of the present invention may be used in a broad range of fragrance applications, e.g. in any field of fine and functional perfumery, such as perfumes, household products, laundry products, body care products and cosmetics. The compounds can be employed in widely varying amounts, depending upon the specific application and on the nature and quantity of other odourant ingredients. The proportion
- 30 is typically from 0.001 to 20 weight percent of the application. In one embodiment, compounds of the present invention may be employed in a fabric softener in an amount of from 0.001 to 0.05 weight percent. In another embodiment, compounds of the present invention may be used in fine perfumery in amounts of from 0.1 to 20 weight percent, more preferably between 0.1 and 5 weight percent. However, these values are

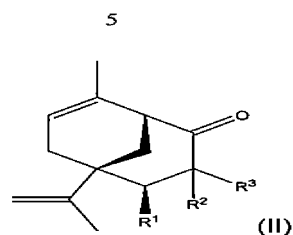
given only by way of example, since the experienced perfumer may also achieve effects or may create novel accords with lower or higher concentrations.

5 The compounds of the present invention may be employed into the fragrance application simply by directly mixing the fragrance composition with the fragrance application, or they may, in an earlier step be entrapped with an entrapment material, for example, polymers, capsules, microcapsules and nanocapsules, liposomes, film formers, absorbents such as carbon or zeolites, cyclic oligosaccharides and mixtures thereof, or they may be chemically bonded to substrates, which are adapted to release
10 the fragrance molecule upon application of an external stimulus such as light, enzyme, or the like, and then mixed with the application.

Thus, the invention additionally provides a method of manufacturing a fragrance application, comprising the incorporation of a compound of formula (I) as a fragrance
15 ingredient, either by directly admixing the compound of formula (I) to the application or by admixing a fragrance composition comprising a compound of formula (I), which may then be mixed to a fragrance application, using conventional techniques and methods.

As used herein, "fragrance application" means any product, such as fine perfumery,
20 e.g. perfume and Eau de Toilette; household products, e.g. detergents for dishwasher, surface cleaner; laundry products, e.g. softener, bleach, detergent; body care products, e.g. shampoo, shower gel; and cosmetics, e.g. deodorant, vanishing creme, comprising an odourant. This list of products is given by way of illustration and is not to be regarded as being in any way limiting.

25 Compounds of formula (I) wherein R⁴ and R⁵ together with the carbon atom to which they are attached form a carbonyl group (see formula (II) below) may be prepared by the reaction of α -pinene with α,β -unsaturated carboxylic acids or derivatives thereof such as alkenoyl halogenide, e.g. crotonyl chloride, crotonyl bromide and pentenoyl
30 chloride; or alkenoyl anhydride, for example crotonic anhydride, in the presence of a catalytic amount of an acid, such as Lewis acid or Bronsted acid.



Surprisingly we have found that certain compounds of formula (I) may also be prepared by reacting α -pinene with β,γ -unsaturated carboxylic acids or β -hydroxy carboxylic acids, resulting in a ketone of formula (II) in the presence of a catalytic amount of an acid. It is believed that, due to the acidic conditions, both the β,γ -unsaturated carboxylic acids and the β -hydroxy carboxylic acids will transfer to the corresponding α,β -unsaturated carboxylic acids, which then will react with α -pinene.

The resulting compounds of formula (II) may be alkylated to give further compounds of formula (I). Still further compounds of formula (I) may be prepared by reduction and/or acylation of the carbonyl group at C2 or by Grignard reaction and acylation of the carbonyl group at C2. Still further compounds of formula (I) may be prepared by hydrogenation.

Compounds of formula (I) wherein either R^2 or R^3 is not hydrogen, and R^4 and R^5 together with the carbon atom to which they are attached form a carbonyl group may also be prepared by the reaction of α -pinene with α,β -unsaturated α -alkyl carboxylic acids, e.g. 2-methylcrotonyl chloride, 2-ethylcrotonyl chloride, 2-methylcrotonic anhydride, in the presence of a catalytic amount of an acid.

Optically pure compounds of formula (I) and enantiomer mixtures of a compound of formula (I) enriched in one enantiomer may be synthesised by starting from the optically pure α -pinene or from an enantiomer mixture enriched in either (S)-(+)- α -pinene or (R)-(-)- α -pinene respectively.

The invention is now further described with reference to the following non-limiting examples.

Example 1: 5-Isopropenyl-4,8-dimethylbicyclo[3.3.1]non-7-en-2-one (1)

- 5 a) A mixture of 30g α -pinene ((1*S*)-(-)/(1*R*)-(+)) 90:10, 0.22mol), 67.8g crotonic anhydride (0.44mol, 2 eq.), and 4.95g zinc bromide (0.021mol, 0.1 eq.) was heated at 95°C for 7h. The reaction mixture was then treated with 50ml H₂O and heated 3h at reflux. Extraction with Et₂O, drying of the org. phases with Na₂SO₄ followed by *Vigreux*-distillation and FC (Flash Chromatography) (SiO₂, hexane/Et₂O 95:5) gave 990mg (2%) of compound **1**. The boiling point of the end product is 80°C at 0.07 torr (0.09 mbar).

10 $[\alpha]_D^{25} = -280.5$ (c=0.93, EtOH)

Odour description: woody, resinous, fir, fruity raspberry ketone-like, olibanum-like, ciste, ambery

- 15 b) According to the procedure described above starting from (-)- α -pinene in the presence of crotonyl chloride at 90°C for 4 hours.

$[\alpha]_D^{25} = -785$ (c=0.75, EtOH)

20 Odour description: fruity, woody, piny, ambery

c) According to the procedure describe above starting from (+)- α -pinene in the presence of crotonic anhydride at 95°C for 6h.

25 $[\alpha]_D^{25} = +536.2$ (c=1.02, EtOH)

Odour description: grapefruit, red fruit, piny, ambery

- 30 ¹H-NMR (400MHz, CDCl₃): δ 5.63-5.59 (br. *m*, H-C(7)), 4.75-4.72 (br. *s*, H_{*r*}-CH=), 4.64-4.62 (br. *s*, H_{*c*}-CH=), 3.08 (*dd*, J = 6.7, 14.5, H _{α} -C(3)), 2.82-2.78 (br. *s*, H-C(1)), 2.45-2.31 (*m*, C(6)H₂), 2.27 (*quintet t*, J = 2.0, 7.0, H-C(4)), 2.18 (*dd*, J = 3.3, 12.8, irradi. at 2.80 → *d*, J = 12.8, H_{*syn*}-C(9)), 1.89 (*dt*, J = 1.6, 14.5, irradi. at 2.80 → *dd*, J = 1.6, 14.0, H_{*r*}-C(3)), 1.87 (*dt*, J = 2.6, 12.8, irradi. at 2.80 → *dd*, J = 2.2, 13.0, H_{*anti*}-C(9)), 1.73 (*s*, MeC=CH₂), 1.66 (br. *s*, J = 1.9, MeC(8)), 0.80 (*d*, J = 7.2, MeC(4)).

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^{13}C -NMR (100MHz, CDCl_3): δ 212.42 (s, CO), 150.75 (s, C(5)C=), 134.36 (s, C(8)), 124.85 (d, C(7)), 108.75 (t, CH_2 =), 53.98 (d, C(1)), 40.92 (t, C(3)), 39.40 (d, C(4)), 39.25 (t, C(6)), 39.17 (s, C(5)), 31.20 (t, C(9)), 21.79 (q, MeC(8)), 18.42 (q, MeC=CH₂), 16.59 (q, MeC(4)).

5 MS (EI): 204 (34), 189 (8), 171 (4), 161 (11), 147 (19), 134 (30), 133 (50), 119 (99), 105 (78), 97 (93), 93 (100), 91 (87), 77 (49), 69 (28), 41(70).

IR: ν_{max} 2954, 2877, 1718, 1659, 1445, 1376, 1311, 1292, 1267, 1182, 1101, 1027, 968, 838, 688 cm^{-1} .

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Example 2: 4-Ethyl-5-isopropenyl-8-methylbicyclo[3.3.1]non-7-en-2-one (2)

At 30°C, a mixture of 7.35g of 2-pentenoyl chloride (62mmol) and 1.7g of zinc chloride (12mmol, 0.2 eq.) in 85ml ethylene chloride was treated dropwise within 20 min. with a
 15 solution of 19.4g of (-)-alpha-pinene (142mmol, 2 eq.) in 20ml ethylene dichloride. The reaction mixture was then stirred at 30°C for 30min., then at 50°C for 2h, and finally at 80°C for 1h. After cooling, the reaction mixture was washed with aq. sat. NaCl soln. and aq. sat. NaHCO₃ soln. The aq. phases were extracted with Et₂O, dried (Na₂SO₄), and concentrated. FC (SiO₂, hexane/Et₂O 20:1) of the crude (26 g) gave 1.74 g (13%) of
 20 compound 2. The boiling point of the end product is 95°C at 0.06 torr (0.08 mbar).

^1H -NMR (400MHz, CDCl_3): δ 5.63-5.60 (tq, J = 1.5, 3.5, H-C(7)), 4.63 (quintet, J = 1.3, H₇-CH=), 4.66-4.65 (br. s, H_c-CH=), 2.93 (ddd, J = 1.6, 6.3, 14.7, H _{α} -C(3)), 2.81-2.78 (br. s, H-C(1)), 2.44-2.30 (m, C(6)H₂), 2.14 (dt, J = 1.6, 14.8, H _{β} -C(3)), 2.09 (dd, J = 3.4,
 25 12.6, H_{syn}-C(9)), 1.89 (dt, J = 2.7, 12.6, H_{anti}-C(9)), 1.88-1.81 (m, H-C(4)), 1.72 (dd, J = 0.6, 1.3, MeC=CH₂), 1.67 (td, J = 1.5, 2.3, MeC(8)), 1.36-1.24 (sext t, J = 1.8, 7.7, 13.5, MeCH-C(4)), 1.03-1.09 (dq, J = 6.2, 7.3, 13.4, MeCH-C(4)), 0.87 (d, J = 7.2, MeCH₂).

^{13}C -NMR (100MHz, CDCl_3): δ 212.75 (s, CO), 151.13 (s, C(5)C=), 134.71 (s, C(8)), 125.04 (d, C(7)), 109.09 (t, CH_2 =), 53.98 (d, C(1)), 47.24 (d, C(4)), 40.07 (s, C(5)),
 30 39.52 (t, C(6)), 36.64 (t, C(3)), 32.19 (t, C(9)), 22.48 (t, CH₂Me), 21.97 (q, MeC(8)), 18.76 (q, MeC=CH₂), 12.77 (q, MeCH₂).

MS (EI): 219 (5), 218 (28), 203 (5), 190 (4), 189 (14), 175 (9), 162 (4), 161 (15), 148 (5), 147 (16), 145 (5), 136 (9), 135 (26), 134 (44), 133 (56), 132 (12), 131 (6), 126 (5), 125 (7), 121 (19), 120 (20), 119 (100), 117 (17), 115 (15), 112 (5), 111 (68), 108 (12), 107

(26), 106 (17), 105 (74), 103 (9), 97 (17), 95 (20), 94 (15), 93 (90), 92 (34), 91 (84), 83 (28), 81 (14), 80 (8), 79 (34), 78 (12), 77 (47), 42 (17), 65 (20), 55 (39), 53 (21), 51 (10), 41 (55), 39 (28), 29 (13), 27 (11).

IR: ν_{\max} 2963, 2928, 2876, 1707, 1678, 1638, 1448, 1379, 1225, 1153, 1089, 1062, 1009, 916, 889, 857, 811, 786, 717 cm^{-1} .

$[\alpha]_D^{25} = -572.7$ (1.07 in EtOH)

Odour description: ambery, woody, spicy

10 Example 3: (1*S**3*S**4*S**5*R**)-5-Isopropenyl-3,4,8-trimethylbicyclo[3.3.1]non-7-en-2-one (3)

At 0°C, 15.3ml of a soln. of LDA (2M in THF/heptane/ethylbenzene, 31mmol, 2.5 eq.) was treated dropwise with a soln. of 2.5 g of 5-Isopropenyl-4,8-dimethyl-
15 bicyclo[3.3.1]non-7-en-2-one (12mmol) in 25ml THF. The reaction mixture was stirred 1.5h at 0°C, treated with 2.6ml methyl iodide (41.7mmol, 3.4 eq.), stirred at 25°C for 3h, and poured into 1M aq. HCl soln. Extraction with MTBE (2 X 80 ml), washing of the org. phase with H₂O, aq. sat. NaCl soln., drying (MgSO₄) gave 3.6 g crude. FC (hexane/MTBE 24:1) gave 0.56g (21%) of compound 3. The boiling point of the end
20 product is 120°C at 0.08 mbar. R_f (hexane/MTBE 24:1) 0.26.

¹H-NMR (400MHz, CDCl₃): δ 5.54-5.50 (*m*, H-C(7)), 4.78 (*quintet*, *J* = 1.3, H_{*r*}-CH=), 4.72-4.70 (*br. s*, H_{*c*}-CH=), 2.82-2.78 (*br. s*, H-C(1)), 2.35-2.22 (*m*, C(6)H₂, H_{*syn*}-C(9), H-C(3)), 1.84 (*dq (quintet)*, *J* = 7.3, H-C(4)), 1.79 (*td*, *J* = 1.6, 2.3, MeC(8)), 1.72 (*dd*, *J* = 0.9, 1.6, MeC=CH₂), 1.70 (*dd*, *J* = 2.3, 13.0, H_{*anti*}-C(9)), 1.20 (*d*, *J* = 7.5, Me-C(3)), 0.86 (*d*, *J* = 7.2, Me-C(4)).

¹H-NMR (400MHz, C₆D₆): δ 5.24-5.20 (*m*, H-C(7)), 4.78 (*quintet*, *J* = 1.4, H_{*r*}-CH=), 4.63-4.60 (*br. s*, H_{*c*}-CH=), 2.71-2.67 (*br. s*, H-C(1)), 2.10-2.03 (*m*, H_{*p*}-C(6)), 2.07 (*dq (quintet)*, *J* = 7.5, H-C(3)), 1.91 (*ddd*, *J* = 1.9, 2.8, 13.0, H_{*syn*}-C(9)), 1.93-1.85 (*ddt*, *J* = 1.8, 4.6, 13.0, H_{*α*}-C(6)), 1.76 (*td*, *J* = 1.6, 2.3, MeC(8)), 1.55 (*dq (quintet)*, *J* = 7.3, H-C(4)), 1.54 (*dd*, *J* = 0.9, 1.6, MeC=CH₂), 1.35 (*dd*, *J* = 2.9, 13.0, H_{*anti*}-C(9)), 1.12 (*d*, *J* = 7.3, Me-C(3)), 0.69 (*d*, *J* = 7.2, Me-C(4)).

¹³C-NMR (100MHz, CDCl₃): δ 212.75 (*s*, CO), 151.01 (*s*, C(5)C=), 132.72 (*s*, C(8)), 124.48 (*d*, C(7)), 109.60 (*t*, CH₂=), 51.98 (*d*, C(1)), 48.25 (*br. d*, C(3)), 41.15 (*br. d*,

C(4)), 39.35 (t, C(6)), 39.33 (s, C(5)), 29.99 (t, C(9)), 21.58 (q), 20.12 (q), 19.50 (br. q), 18.22 (q).

^{13}C -NMR (100MHz, C_6D_6): δ 210.1 (s, CO), 151.0 (s, C(5)C=), 133.3 (s, C(8)), 123.9 (d, C(7)), 110.1 (t, CH_2 =), 51.8 (d, C(1)), 47.4 (br. d, C(3)), 40.6 (br. d, C(4)), 39.7 (s, C(5)), 39.4 (t, C(6)), 30.2 (t, C(9)), 21.8 (q, Me-C(8)), 20.6 (q, MeC=CH₂), 17.9 (br. q, Me-C(3)), 17.6 (q, Me-C(4)).

MS (EI): 218 (27), 203 (8), 190 (8), 185 (3), 175 (8), 161 (11), 147 (19), 133 (66), 119 (100), 111 (47), 107 (47), 105 (72), 93 (72), 91 (76), 83 (57), 77 (43), 65 (18), 55 (48), 41 (62).

IR: ν_{max} 2969, 2934, 1708, 1636, 1448, 1376, 1233, 1155, 1092, 1061, 1040, 994, 955, 919, 890, 814, 781, 734, 649 cm^{-1} .

$[\alpha]_D^{25} = -655.3$ (c=0.99, EtOH)

Odour description: woody, green, floral, rosy, ambery

Example 4: 5-Isopropenyl-3,3,4,8-tetramethylbicyclo[3.3.1]non-7-en-2-one (4)

At 55°C, a mixture of 9.9g KOH (176 mmol, 15 eq.) in 40ml DMSO was treated dropwise with a soln. of 2.4g of 5-isopropenyl-4,8-dimethyl-bicyclo[3.3.1]non-7-en-2-one (11.7mmol) in 3.7ml methyl iodide (59mmol, 5 eq.). The reaction mixture was stirred 1.5h at 60°C, treated with 2.0ml methyl iodide (32mmol, 2.7 eq.), stirred at 60°C for 1.5h, treated with 1.7ml methyl iodide (27mmol, 2.3 eq.), stirred at 60°C for 1.5h, cooled, and poured into 200ml of 2M aq. HCl soln. Extraction with hexane (2 X 100ml), washing of the org. phase with H₂O, aq. sat. NaCl soln., drying (MgSO₄) gave 2.6g crude. FC (hexane/MTBE 15:1) gave 0.7g (26%) of compound 4. The boiling point of the end product is 120°C at 0.08 mbar. R_f (hexane/MTBE 15:1) 0.27.

^1H -NMR (400MHz, CDCl_3): δ 5.55-5.51 (m, H-C(7)), 4.83 (quintet, J = 1.4, H_C-CH=), 4.75-4.73 (br. s, H_C-CH=), 2.86-2.83 (m, H-C(1)), 2.43-2.35 (m, H-C(6)), 2.33-2.25 (m, H-C(6)), 2.28 (ddd, J = 1.6, 3.0, 13.0, H_{anti}-C(9)), 1.96 (qd, J = 1.0, 7.4, H-C(4)), 1.80 (dd, J = 0.5, 1.3, MeC=CH₂), 1.70 (dd, J = 1.1, 13.0, H_{syn}-C(9)), 1.70 (q, J \approx 1.8, MeC(8)), 1.21 (s, Me), 1.07 (s, Me), 0.85 (d, J = 7.5, MeC(4)).

¹³C-NMR (100MHz, CDCl₃): δ 214.58 (s, CO), 151.65 (s, C(5)C=), 133.10 (s, C(8)), 124.94 (d, C(7)), 109.91 (t, CH₂=), 52.58 (d, C(1)), 47.15 (s, C(3)), 45.15 (d, C(4)), 40.64 (s, C(5)), 40.49 (t, C(6)), 31.33 (q), 30.55 (t, C(9)), 25.21 (q), 22.18 (q), 21.44 (q), 13.95 (q).

5 MS (EI): 218 (27), 203 (8), 190 (8), 185 (3), 175 (8), 161 (11), 147 (19), 133 (66), 119 (100), 111 (47), 107 (47), 105 (72), 93 (72), 91 (76), 83 (57), 77 (43), 65 (18), 55 (48), 41 (62).

IR: ν_{max} 2969, 2934, 1708, 1636, 1448, 1376, 1233, 1155, 1092, 1061, 1040, 994, 955, 919, 890, 814, 781, 734, 649 cm⁻¹.

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Odour description: woody, ambery

Example 5: (1*S**4*S**5*R**)-5-Isopropenyl-8,8-dimethoxy-2,6-dimethylbicyclo[3.3.1]non-2-ene (5)

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A soln. of 1.5g of 5-isopropenyl-4,8-dimethylbicyclo[3.3.1]non-7-en-2-one (7.3mmol), 1.4g para-toluenesulfonic acid mono hydrate (7.4mmol 1 eq.), and 0.78g trimethyl-orthoformate (7.4mmol, 1 eq.) in 50ml methanol was heated at 60°C for 66h. The reaction mixture was then cooled and poured into aq. sat. NaHCO₃ soln. (20ml). Extraction with MTBE (2 X 80 ml) followed by washing of the aq. phases with H₂O and aq. sat. NaCl soln., drying of org. phases (MgSO₄) led to 1.8g of crude product. FC (SiO₂, Hexane/MTBE 30:1) gave 1.7 g (92%) of compound **5** as colorless liquid. The boiling point of the end product is 130°C at 0.08 mbar. R_f (hexane/MTBE 8:1) 0.57.

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¹H-NMR (400MHz, CDCl₃): δ 5.48 (tq, J = 1.4, 3.7, H-C(7)), 4.63 (quintet, J = 1.4, H-CH=), 4.61-4.60 (br. s, H_c-CH=), 3.20 (s, OMe), 3.17 (s, OMe), 2.49-2.45 (m, irradi. at 1.43 → changes, H-C(1)), 2.17-2.02 (m, C(6)H₂), 1.97 (dd, J = 3.0, 12.4, irradi. at 1.43 → br. d, J ≈ 4.0, H_{syn}-C(9)), 1.88 (dd, J ≈ 6.2, 14.4, H_α-C(3)), 1.90-1.81 (m, irradi. at 1.43 → changes, H-C(4)), 1.79 (td, J = 1.7, 2.1, MeC(8)), 1.66 (dd, J = 0.6, 1.4, MeC=CH₂), 1.69-1.61 (m, irradi. at 2.47 → changes, H_β-C(3)), 1.43 (ddd, J = 1.6, 3.5, 12.5, irradi. at 2.47 → dd, J = 1.4, 12.6, H_{anti}-C(9)), 0.88 (d, J = 7.7, MeC(4)).

30

¹H-NMR (400MHz, C₆D₆): δ 5.49-5.45 (m, H-C(7)), 4.77-4.73 (m, CH₂=), 3.05 (s, OMe), 3.03 (s, OMe), 2.49-2.44 (m, H-C(1)), 2.12-2.05 (m, H-C(6)), 2.05 (dd, J = 2.8, 12.3,

- $H_{syn}\text{-C(9)}$), 1.96 (*td*, $J = 1.7, 2.1$, MeC(8)), 1.99-1.91 (*m*, H-C(6)), 1.93 (*dd*, $J = 6.2, 13.5$, $\text{H}_{\alpha}\text{-C(3)}$), 1.71 (*quintet t*, $J = 1.7, 7.2$, H-C(4)), 1.63 (*dt*, $J = 1.9, 13.5$, $\text{H}_{\beta}\text{-C(3)}$), 1.61 (*dd*, $J = 0.6, 1.2$, MeC=CH_2), 1.48 (*ddd*, $J = 1.8, 3.5, 12.4$, $\text{H}_{anti}\text{-C(9)}$), 1.06 (*d*, $J = 7.3$, MeC(4)).
- 5 $^{13}\text{C-NMR}$ (100MHz, CDCl_3): δ 152.59 (*s*, C(5)C=), 135.79 (*s*, C(8)), 124.07 (*d*, C(7)), 107.32 (*t*, $\text{CH}_2\text{=}$), 102.98 (*s*, C(2)), 47.59 (*q*, OMe), 47.47 (*q*, OMe), 40.59 (*d*), 40.14 (*t*, C(6)), 39.12 (*s*, C(5)), 37.05 (*d*), 32.53 (*t*, C(9)), 27.90 (*t*, C(3)), 24.45 (*q*), 18.33 (*q*), 17.41 (*q*).
- 10 $^{13}\text{C-NMR}$ (100MHz, C_6D_6): δ 152.71 (*s*, C(5)C=), 136.37 (*s*, C(8)), 124.13 (*d*, C(7)), 107.78 (*t*, $\text{CH}_2\text{=}$), 103.25 (*s*, C(2)), 47.46 (*q*, OMe), 46.38 (*q*, OMe), 40.90 (*d*), 40.61 (*t*, C(6)), 39.65 (*s*, C(5)), 37.47 (*d*), 33.36 (*t*, C(9)), 27.30 (*t*, C(3)), 24.97 (*q*), 18.57 (*q*), 18.02 (*q*).
- MS (EI): 250 (0.2), 218 (31), 203 (19), 187 (5), 171 (12), 137 (57), 115 (100), 91 (35), 77 (23), 69 (15), 55 (16), 41 (35).
- 15 IR: ν_{max} 2945, 2829, 1638, 1451, 1366, 1308, 1194, 1160, 1130, 1110, 1086, 1051, 1018, 972, 953, 922, 886, 846, 799, 772 cm^{-1} .
- $[\alpha]_D^{25} = -150.1$ ($c=1.00$, EtOH)

Odour description: ambery, woody, fruity, sweet

20

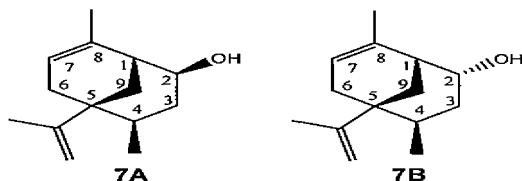
Example 6: (1*S**4*S**5*R**)- 4,8-Dimethyl-5-isopropenylspiro[bicyclo[3.3.1]nonane-2,2'-[1,3]dioxolane] (6)

- 25 A soln. of 2.0g of 5-isopropenyl-4,8-dimethylbicyclo[3.3.1]non-7-en-2-one (9.8mmol) in 100ml cyclohexane was treated with 1.8g ethyleneglycol (2.9mmol, 3.0 eq.) and 0.2g para-toluenesulfonic acid mono hydrate (1.0mmol 0.1 eq.). The soln. obtained was heated at reflux for 3h (Dean-Stark apparatus), cooled and poured into aq. sat. NaHCO_3 soln. (100ml). Extraction with MTBE (2 x 80ml) followed by washing of the aq. phases
- 30 with H_2O (100ml) and aq. sat. NaCl soln. (150ml), drying of org. phases over MgSO_4 led to 2.6g of crude product. FC (SiO_2 , hexane/MTBE 19:1) gave 0.76g (31%) of compound **6** as colorless liquid. The boiling point of the end product is 130°C at 0.09 mbar. R_f (hexane/MTBE 19:1) 0.47.

- ¹H-NMR (400MHz, CDCl₃): δ 5.49 (*tg*, J = 1.4, 3.5, H-C(7)), 4.64 (*quintet*, J = 1.4, H-C(1)-CH=), 4.62-4.60 (*br. s*, H-C-CH=), 4.03-3.88 (*m*, OCH₂CH₂O), 2.21-2.18 (*br. s*, H-C(1)), 2.17 (*dd*, J = 6.2, 13.8, H α -C(3)), 2.14-2.09 (*m*, C(6)H₂), 2.09 (*dd*, J = 2.9, 12.9, H_{syn}-C(9)), 1.92 (*quintet t*, J = 1.7, 7.2, H-C(4)), 1.79 (*td*, J = 1.5, 2.2, MeC(8)), 1.66 (*dd*, J = 0.6, 1.3, MeC=CH₂), 1.52 (*ddd*, J = 1.9, 3.4, 12.6, H_{anti}-C(9)), 1.36 (*dt*, J = 1.8, 13.9, H β -C(3)), 0.89 (*d*, J = 7.2, MeC(4)).
- ¹³C-NMR (100MHz, CDCl₃): δ 152.43 (*s*, C(5)C=), 135.84 (*s*, C(8)), 123.96 (*d*, C(7)), 111.52 (*s*, C(2)), 107.53 (*t*, CH₂=), 64.27 (*t*, OCH₂), 63.46 (*t*, OCH₂), 43.56 (*d*), 39.89 (*t*, C(6)), 38.92 (*s*, C(5)), 37.34 (*d*), 34.16 (*t*, C(9)), 28.70 (*t*, C(3)), 23.97 (*q*), 18.32 (*q*), 16.88 (*q*).
- MS (EI): 248 (1), 233 (0.2), 203 (0.3), 147 (2), 133 (3), 119 (5), 113 (100), 105 (6), 91 (9), 86 (4), 77 (5), 69 (9), 41 (9).
- IR: ν_{max} 2962, 2885, 1638, 1450, 1368, 1308, 1162, 1129, 1110, 1083, 1063, 1042, 1020, 975, 953, 925, 887, 845, 831, 801 cm⁻¹.
- $[\alpha]_D^{25} = -142.8$ (c=0.51, EtOH)

Odour description: fruity, spicy, woody

Example 7: 5-Isopropenyl-4,8-dimethylbicyclo[3.3.1]non-7-en-2-ol (7A and 7B)



- At 5°C, a soln. of 1g of 5-isopropenyl-4,8-dimethylbicyclo[3.3.1]non-7-en-2-one (4.9mmol) in 5ml ethanol was treated with 0.37g NaBH₄ (9.8mmol, 2 eq.). The reaction mixture was then stirred 2h at 25°C, poured into 1N aq. HCl soln., and extracted with Et₂O. The org. phase was washed with aq. sat. NaCl soln., dried, and concentrated. FC

(hexane/Et₂O 9:1 to 9:2) of the crude (1g, **7A/7B** 30:70) gave 0.1 g **7A** (10%), 0.2 g **7A/7B** (1:1, 20%), and 0.4 g **7B** (40%).

(1S*2R*4S*5R*)-5-Isopropenyl-4,8-dimethylbicyclo[3.3.1]non-7-en-2-ol (**7A** (exo))

5

Boiling point: 100°C at 0.06 torr (0.08mbar).

¹H-NMR (400MHz, CDCl₃): δ 5.44 (*tq*, J = 1.4, 3.5, H-C(7)), 4.67-4.64 (*m*, C=CH₂), 3.90 (*dt*, J = 2.8, 2.9, H-C(2)), 2.29-2.25 (*m*, H-C(1)), 2.20 (*dd*, J = 3.0, 12.6, H_{syn}-C(9)), 2.10-2.05 (*m*, C(6)H₂), 2.02 (*ddd*, J = 3.7, 6.2, 14.9, H_α-C(3)), 1.82-1.75 (*m*, H-C(4)), 1.69 (*td*, J = 1.6, 2.1, MeC(8)), 1.66 (*dd*, J = 0.6, 1.1, MeC=CH₂), 1.45 (*ddt*, J = 1.6, 1.8, 14.8, H_β-C(3)), 1.37 (*ddd*, J = 1.2, 1.7, 12.6, H_{anti}-C(9)), 0.98 (*d*, J = 7.3, MeC(4)).

¹³C-NMR (100MHz, CDCl₃): δ 152.93 (*s*, C(5)C=), 135.27 (*s*, C(8)), 123.66 (*d*, C(7)), 107.21 (*t*, CH₂=), 68.41 (*d*, C(2)), 43.39 (*d*), 39.36 (*t*, C(6)), 39.18 (*s*, C(5)), 35.96 (*d*), 32.99 (*t*, C(9)), 24.12 (*t*, C(3)), 22.26 (*q*, MeC(8)), 18.87 (*q*, MeC=CH₂), 17.91 (*q*, MeC(4)).

MS (EI): 206 (17), 188 (44), 173 (32), 159 (14), 147 (19), 145 (26), 133 (58), 119 (66), 107 (71), 105 (77), 93 (100), 77 (50), 71 (24), 55 (36), 41 (70).

[α]_D²⁵ = -141.4 (c=0.89, EtOH)

20

Odour description: floral, agrestic, rosy, green

(1S*2S*4S*5R*)-5-Isopropenyl-4,8-dimethylbicyclo[3.3.1]non-7-en-2-ol (**7B**(endo))

25 Boiling point: 80°C at 0.05 torr (0.07mbar).

¹H-NMR (400MHz, CDCl₃): δ 5.60 (*tq*, J = 1.5, 3.5, H-C(7)), 4.63 (*quintet*, J = 1.4, H_β-CH=), 4.58-4.56 (*br. s*, H_β-CH=), 4.03 (*dt*, J = 4.4, 11.5, irradi. at 2.48 → *dd*, J ≈ 4.4, 11.2, H-C(2)), 2.50-2.45 (*m*, irradi. at 4.03 → changes, H-C(1)), 2.12-2.00 (*br. s*, C(6)H₂), 1.89 (*br. quintet t*, J = 1.7, 7.1, H-C(4)), 1.86-1.76 (*m*, irradi. at 4.03 → changes, irradi. at 2.48 → changes, H_{syn}-C(9), H_α-C(3)), 1.81 (*td*, J = 1.6, 2.2, MeC(8)), 1.64 (*br. d*, J = 0.8, MeC=CH₂), 1.57 (*ddd*, J = 1.8, 3.7, 12.8, irradi. at 2.48 → *dd*, J ≈ 2.0, 12.8, H_{anti}-C(9)), 1.55 (*dddd*, J = 1.4, 1.8, 4.4, 12.4, irradi. at 4.03 → *dt*, J ≈ 1.9, 11.6, irradi. at 2.48 → *dd*, J = 2.0, 4.4, 12.4, H_β-C(3)), 1.33-1.21 (*br. s*, OH), 0.80 (*d*, J = 7.2, MeC(4)).

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¹H-NMR (400MHz, C₆D₆): δ 5.52 (*td*, *J* = 1.5, 3.4, H-C(7)), 4.68 (*quintet*, *J* = 1.4, H_{*r*}-CH=), 4.63-4.61 (*br. s*, H_{*c*}-CH=), 3.73 (*dt*, *J* = 4.4, 11.6, H-C(2)), 2.29-2.25 (*m*, H-C(1)), 2.03-1.95 (*m*, H-C(6)), 1.91 (*td*, *J* = 1.6, 2.1, MeC(8)), 1.88-1.80 (*m*, H-C(6)), 1.77 (*td*, *J* = 5.3, 12.2, H_{*c*}-C(3)), 1.61 (*br. quintet t*, *J* = 1.8, 7.2, H-C(4)), 1.62-1.57 (*m*, H_{*syn*}-C(9)), 1.52 (*dd*, *J* = 0.6, 1.3, MeC=CH₂), 1.49 (*ddd*, *J* = 1.8, 3.7, 12.7 H_{*anti*}-C(9)), 1.30 (*dddd*, *J* = 1.3, 2.0, 4.4, 12.6, H_{*r*}-C(3)), 0.71 (*d*, *J* = 7.2, MeC(4)), 0.66-0.57 (*br. s*, OH).

¹³C-NMR (100MHz, CDCl₃): δ 152.26 (*s*, C(5)C=), 133.63 (*s*, C(8)), 124.24 (*d*, C(7)), 107.48 (*t*, CH₂=), 69.53 (*d*, C(2)), 42.84 (*d*), 39.94 (*t*, C(6)), 38.64 (*s*, C(5)), 37.23 (*d*), 34.61 (*t*, C(9)), 29.57 (*t*, C(3)), 25.05 (*q*, MeC(8)), 18.26 (*q*, MeC=CH₂), 16.15 (*q*, MeC(4)).

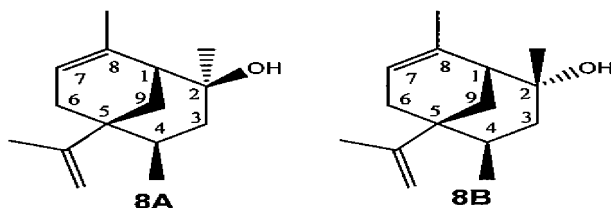
MS (EI): 206 (17), 188 (44), 173 (32), 159 (14), 147 (19), 145 (26), 133 (58), 119 (66), 107 (71), 105 (77), 93 (100), 77 (50), 71 (24), 55 (36), 41 (70).

IR: ν_{\max} 3282, 2966, 2933, 2880, 1637, 1443, 1375, 1355, 1329, 1296, 1250, 1162, 1079, 1047, 1029, 998, 887, 821, 792, 632 cm⁻¹.

$[\alpha]_D^{25} = -226.0$ (*c*=0.98, EtOH)

Odour description: floral, isononanol-like, grapefruit

Example 8: 5-Isopropenyl-2,4,8-trimethylbicyclo[3.3.1]non-7-en-2-ol (8A and 8B)



At 5°C, a soln. of 1g of 5-isopropenyl-4,8-dimethylbicyclo[3.3.1]non-7-en-2-one (4.9mmol) in 15ml THF was treated dropwise with 21ml 1.4M MeLi in Et₂O (29.4mmol, 6 eq.). The reaction mixture was stirred 5h at 5°C, warmed to 25°C overnight, poured into aq. sat. NH₄Cl soln., and extracted with Et₂O. The org. phase was washed with aq. sat. NaCl soln., dried, and concentrated. FC (SiO₂, hexane/Et₂O 9:1) of the crude (1.2g,

starting material/OH exo/OH endo 17:65:18) gave 0.2g of starting material (20%), 0.5 g **8A** (46%), 0.25 g **8A/8B** (1:1, 23%), and 0.1 g **8B** (9%).

(1S*2R*4S*5R*)-5-Isopropenyl-2,4,8-trimethylbicyclo[3.3.1]non-7-en-2-ol (**8A**(exo))

5

Boiling point: 80°C at 0.07 torr (0.09mbar).

¹H-NMR (400MHz, CDCl₃): δ 5.44 (*tq*, J = 1.5, 3.7, H-C(7)), 4.66-4.64 (br. s, H_c-CH=), 4.63 (*quintet*, J = 1.4, H_f-CH=), 2.26 (*dd*, J = 3.1, 12.5, H_{syn}-C(9)), 2.10-2.05 (*m*, C(6)H₂, H-C(1)), 1.92 (*dd*, J = 6.1, 14.4, H_α-C(3)), 1.81 (*quintet t*, J = 1.5, 7.2, H-C(4)), 1.77 (*td*, J = 1.5, 2.2, MeC(8)), 1.67 (*dd*, J = 0.6, 1.3, MeC=CH₂), 1.38 (*ddd*, J = 1.5, 3.0, 12.5, H_{anti}-C(9)), 1.31 (*dt*, J = 1.6, 14.4, H_β-C(3)), 1.27-1.21 (br. s, OH), 1.18 (s, MeC(2)), 0.98 (d, J = 7.3, MeC(4)).

¹³C-NMR (100MHz, CDCl₃): δ 152.70 (s, C(5)C=), 135.83 (s, C(8)), 124.48 (d, C(7)), 107.11 (t, CH₂=), 73.24 (s, C(2)), 47.84 (d, C(1)), 39.91 (t, C(6)), 38.86 (s, C(5)), 38.49 (t), 36.85 (d, C(4)), 31.31 (q, MeC(2)), 26.92 (t), 24.57 (q, MeC(8)), 18.06, 18.03 (2q, MeC=CH₂, MeC(4)).

MS (EI): 220 (6), 202 (22), 187 (18), 162 (48), 147 (21), 135 (56), 119 (55), 107 (66), 93 (74), 85 (100), 77 (39), 67 (26), 55 (28), 43 (81).

IR: ν_{max} 3417, 2968, 2928, 2833, 1640, 1446, 1372, 1329, 1302, 1210, 1151, 1121, 1104, 1033, 942, 926, 886, 832, 800, 781 cm⁻¹.

Odour description: fruity, agrestic, rosy, earthy

(1S*2S*4S*5R*)-5-Isopropenyl-2,4,8-trimethylbicyclo[3.3.1]non-7-en-2-ol (**8B**(endo))

25

Boiling point: 60°C at 0.06 torr (0.08mbar).

¹H-NMR (400MHz, CDCl₃): δ 5.56 (*tq*, J = 1.6, 3.5, H-C(7)), 4.62 (*quintet*, J = 1.4, H_f-CH=), 4.60-4.58 (br. s, H_c-CH=), 2.18-2.14 (*m*, H-C(1)), 2.13-2.08 (*m*, C(6)H₂), 1.97 (*dd*, J = 6.3, 13.1, H_α-C(3)), 1.90 (*quintet t*, J = 1.5, 7.2, H-C(4)), 1.86 (*dd*, J = 3.0, 13.1, H_{syn}-C(9)), 1.84 (*td*, J = 1.5, 2.2, MeC(8)), 1.54 (*ddd*, J = 1.8, 3.5, 13.1, H_{anti}-C(9)), 1.42 (*dt*, J = 1.4, 13.0, H_β-C(3)), 1.41-1.39 (br. s, MeC=CH₂), 1.32-1.22 (br. s, OH), 1.26 (s, MeC(2)), 0.83 (d, J = 7.5, MeC(4)).

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- ¹³C-NMR (100MHz, CDCl₃): δ 152.13 (s, C(5)C=), 135.70 (s, C(8)), 124.14 (d, C(7)), 107.24 (t, CH₂=), 73.32 (s, C(2)), 47.42 (d, C(1)), 40.90, 40.27 (2t, C(3), C(6)), 38.71 (s, C(5)), 37.23 (d, C(4)), 29.24 (t), 29.02 (q, MeC(2)), 25.46 (q, MeC(8)), 18.18, 17.49 (2q, MeC=CH₂, MeC(4)).
- 5 MS (EI): 220 (4), 202 (24), 187 (16), 162 (46), 147 (22), 135 (56), 119 (55), 107 (66), 93 (74), 85 (100), 77 (39), 67 (26), 55 (28), 43 (81).
IR: ν_{max} 3452, 2924, 2881, 1638, 1448, 1376, 1289, 1258, 1160, 1140, 1109, 1061, 1019, 943, 931, 907, 887, 829, 800, 656 cm⁻¹.
- 10 Odour description: fruity, rosy

Example 9: 5-Isopropyl-4,8-dimethylbicyclo[3.3.1]nonan-2-one (9)

- 15 At 25°C, a mixture of 1 g 5-isopropenyl-4,8-dimethylbicyclo[3.3.1]non-7-en-2-one (4.9mmol) and 50mg 10% Pd/C in 10ml MeOH was stirred under 10bar of H₂ for 5h. Filtration (Celite®), concentration, and FC (SiO₂, hexane/Et₂O 100:7) gave 0.22g (22%) of compound **9**. The boiling point of the end product is 75°C at 0.07 torr (0.09mbar).
- 20 ¹H-NMR (400MHz, CDCl₃): δ 2.69 (dd, J = 8.2, 17.4, H _{α} -C(3)), 2.38-2.31 (br. s, H-C(1)), 2.20 (br. d, J = 17.1, H _{β} -C(3)), 2.23-2.12 (m, 1H), 1.79-1.38 (m, 8H), 0.93 (d, J = 7.1, Me), 0.88 (d, J = 6.8, Me), 0.84 (d, J = 6.2, Me), 0.82 (d, J = 6.5, Me).
¹H-NMR (400MHz, C₆D₆): δ 2.39 (dd, J = 8.1, 17.2, H _{α} -C(3)), 2.31-2.26 (m, H-C(1)), 2.12 (br. d, J = 17.3, H _{β} -C(3)), 1.73 (br. quintet, J = 7.1, H-C(4)), 1.53-1.41 (m, H_{anti}-C(9), H-C(7)), 1.40-1.30 (m, H-C(6), H-C(8), CHMe₂), 1.29 (dt, J = 2.3, 13.5, H_{anti}-C(9)), 1.23-1.10 (m, H-C(7), H-C(6)), 0.62 (d, J = 6.7, MeC(8)), 0.69 (d, J = 6.8, MeCHMe), 0.68 (d, J = 7.2, MeC(4)), 0.62 (d, J = 6.9, MeCHMe).
- 25 ¹³C-NMR (100MHz, CDCl₃): δ 214.61 (s, CO), 52.70 (d), 49.67 (t), 37.65 (d), 35.51 (s), 34.33 (d), 33.36 (t), 32.98 (d), 29.93 (t), 28.19 (t), 19.86 (q), 18.34 (q), 17.11 (q), 15.84 (q).
- 30 ¹³C-NMR (100MHz, C₆D₆): δ 210.00 (s, CO), 52.88 (d, C(1)), 49.86 (t, C(3)), 37.68 (d, C(4)), 35.72 (s, C(5)), 34.50 (d, C(8)), 33.51 (t, C(9)), 33.17 (d, CHMe₂), 30.25 (t, C(7)), 28.44 (t, C(6)), 20.23 (q, Me-C(8)), 18.38 (q, Me-C(4)), 17.28, 16.03 (2q, Me₂C).

MS (EI): 208 (22), 193 (7), 190 (3), 165 (36), 147 (14), 137 (58), 123 (24), 109 (15), 95 (84), 81 (100), 67 (30), 55 (36), 41 (45).

$[\alpha]_D^{25} = -108.8$ (c=1.06, EtOH)

- 5 Odour description: fruity, agrestic, rosy, woody

Example 10: (1*S5*R**)-5-Isopropenyl-8-methylbicyclo[3.3.1]non-7-en-2-one (10)**

- 10 A mixture of 20.0 g acryloyl chloride (0.22 mol) and 3.01 g zinc chloride (0.02 mol, 0.1 eq.) in 150 ml ethylene chloride was treated with a soln. of 350 ml α -pinene ((1*S*)-(-)/(1*R*)-(+)) 90:10, 2.20 mol, 10 eq.) in 250 ml ethylene chloride and the resulting mixture was stirred 1 h at 25°C and 4 h at 50°C. After cooling, the reaction mixture was washed with aq. sat. NaCl soln. and aq. sat. NaHCO₃ soln. The aq. phases were extracted with
15 Et₂O, dried (Na₂SO₄), and concentrated. The crude product (48 g) was filtered (SiO₂, hexane/Et₂O 200:6→200:10) and the residue (1.42 g) treated with 300 mg LiOH·H₂O in 15 ml MeOH at 25°C for 7h. The resulting mixture was poured into aq. sat. NaCl soln., extracted with hexane and the org. phases dried with Na₂SO₄. FC (SiO₂, hexane/Et₂O 30:1) gave 347 mg (0.8%) of compound **10**. Boiling point: 80°C at 0.07 torr (0.09mbar).

- 20 ¹H-NMR (400MHz, CDCl₃): δ 5.65 (*tq*, J = 1.5, 3.3, H-C(7)), 4.5-4.743 (br. *s*, H_C-CH=), 4.72 (*quintet*, J = 1.4, H_C-CH=), 2.85 (br. *t*, J = 3.1, H-C(1)), 2.79 (*ddd*, J = 6.8, 13.7, 15.4, H _{α} -C(3)), 2.375 (br. *d*, J = 18.8, H-C(6)), 2.295 (*dddd*, J = 1.9, 3.9, 5.8, 18.9, H-C(6)), 2.12 (*dddd*, J = 1.3, 2.2, 5.9, 15.3, H _{β} -C(3)), 2.13-2.06 (*m*, H _{α} -C(4)), 2.03-2.00
25 (br. *s*, C(9)H₂), 1.78 (*dd*, J = 0.7, 1.3, MeC=CH₂), 1.73 (*dddd*, J = 1.5, 6.0, 13.4, H-C _{β} (4)), 1.67 (*dt*, J = 1.6, 2.2, MeC(8)).

¹³C-NMR (100MHz, CDCl₃): δ 212.05 (*s*, CO), 152.28 (*s*, C(5)C=), 133.76 (*s*, C(8)), 125.20 (*d*, C(7)), 108.06 (*t*, CH₂=), 53.65 (*d*, C(1)), 38.13 (*t*), 36.68 (*t*), 36.00 (*s*, C(5)), 35.64 (*t*), 34.25 (*t*), 21.99 (*q*, MeC(8)), 19.06 (*q*, MeC=CH₂).

- 30 MS (EI): 190 (16), 175 (5), 162 (1), 157 (4), 147 (9), 133 (27), 119 (28), 105 (58), 98 (21), 93 (100), 91 (65), 83 (95), 77 (37), 65 (17), 55 (20), 41(42).

IR: ν_{max} 2929, 1737, 1712, 1637, 1443, 1379, 1241, 1151, 1119, 1058, 993, 890, 789 cm⁻¹.

$[\alpha]_D^{25} = -55.0$ (c=0.79, EtOH)

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Odour description: woody (pine, cedarwood), ambery, sweet

Example 11: (1*S3*R**4*S**5*R**)-5-Isopropenyl-3,4,8-trimethylbicyclo[3.3.1]non-7-en-2-one (11)**

Method a) A mixture of 11.81 g 2-methyl-but-2-enoyl chloride (0.10 mol) and 1.36 g zinc chloride (0.01 mol, 0.1 eq.) in 100 ml ethylene chloride was treated with a soln. of 136 g α -pinene ((1*S*)-(-)/(1*R*)-(+)) 90:10, 1 mol, 10 eq.) in 150 ml ethylene chloride and the resulting mixture was stirred 45 min. at 25°C, 2.5 h at 50°C, and 1 h at 80°. After cooling, the reaction mixture was washed with aq. sat. NaCl soln. and aq. sat. NaHCO₃ soln. The aq. phases were extracted with Et₂O, dried (Na₂SO₄), and concentrated. The crude product (48 g) filtered (SiO₂, hexane/Et₂O 200:6→200:13) and the residue (5.1 g) treated with 1g LiOH·H₂O in 75 ml MeOH at 25°C for 48h. The resulting mixture was poured into aq. sat. NaCl soln. and extracted with hexane. The combined org. phases were dried (Na₂SO₄), concentrated and purified by FC (SiO₂, hexane/Et₂O 100:3) gave 1.6 g (7.1%) of compound **11**.

Method b) 15 ml of a soln. of 0.116 M of EtONa in EtOH were treated with 1.5 g of 5-isopropenyl-3,4,8-trimethylbicyclo[3.3.1]non-7-en-2-one and heated 4 h at reflux. The resulting mixture was poured into 50 ml 2M aq. HCl and extracted with 2X50 ml MTBE. The org. phases were washed with 50 ml H₂O, 50 ml aq. sat. NaCl soln., and dried. FC (SiO₂, hexane/MTBE 20:1) gave 0.75 g (50%) of compound **11**. Boiling point: 80°C at 0.08 mbar.

¹H-NMR (400MHz, CDCl₃): δ 5.61 (*td*, J = 1.5, 3.2, H-C(7)), 4.73 (*quintet*, J = 1.3, H_C-CH=), 4.64-4.62 (*br. s*, H_C-CH=), 3.26 (*qd*, J = 5.8, 6.7, H-C(3)), 2.83 (*br. t*, J = 3.1, H-C(1)), 2.45-2.33 (*m*, C(6)H₂), 2.13 (*qdd*, J = 2.5, 5.6, 7.0, H-C(4)), 2.11 (*dd*, J = 3.4, 12.6, H_{syn}-C(9)), 1.85 (*dt*, J = 2.7, 12.6, H_{anti}-C(9)), 1.72 (*dd*, J = 0.8, 1.2, MeC=CH₂), 1.66 (*dt*, J = 1.6, 2.3, MeC(8)), 0.93 (*d*, J = 6.7, MeC(3)), 0.63 (*d*, J = 7.1, MeC(4)).
¹³C-NMR (100MHz, CDCl₃): δ 214.66 (*s*, CO), 151.19 (*s*, C(5)C=), 135.89 (*s*, C(8)), 124.96 (*d*, C(7)), 108.94 (*t*, CH₂=), 54.02 (*d*, C(1)), 46.01 (*t*, C(3)), 40.96 (*s*, C(5)), 39.47 (*t*, C(6)), 39.30 (*d*, C(4)), 32.16 (*t*, C(9)), 22.21 (*q*, MeC(8)), 18.63 (*q*, MeC=CH₂), 12.38, 10.51 (*2q*, MeC(3), MeC(4)).

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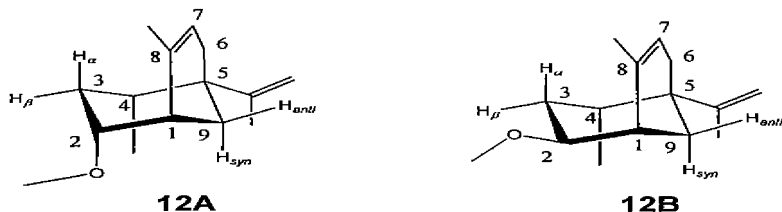
MS (EI): 218 (27), 203 (7), 190 (8), 175 (9), 161 (12), 147 (17), 133 (59), 119 (100), 105 (75), 95 (13), 93 (67), 91 (85), 77 (52), 69 (7), 55 (65), 41 (65).

IR: ν_{\max} 2968, 2927, 1708, 1677, 1638, 1446, 1381, 1351, 1238, 1210, 1152, 1103, 1083, 1059, 1003, 889, 830, 802, 790, 659 cm^{-1} .

5 $[\alpha]_D^{25} = -768.6$ ($c=0.97$, EtOH)

Odour description: fruity, peppery, woody, elemi, gurjun, ambery

Example 12: 4,8-Dimethyl-5-isopropenyl-8-methoxy-bicyclo[3.3.1]non-7-ene (12A and 12B)



A soln. of 2.9 g of 5-isopropenyl-4,8-dimethylbicyclo[3.3.1]non-7-en-2-ol (14.1 mmol, α/β 58:42) in 30 ml DMF was added dropwise to a suspension of 0.84 g 55-65% sodium hydride (21 mmol, 1.5 eq.) in 30 ml DMF and the resulting mixture was stirred 1.5 h at 25°C, treated with 2.6 ml methyl iodide (41.8 mmol, 3 eq.), heated 4.5 h at 80°C, poured into 50 ml HCl 2M, and extracted with 2X80 ml hexane. The org. phases were washed with 2X100 ml 1:1 aq. sat. NaCl soln./H₂O, dried, and concentrated. FC (hexane/MTBE 15:1) of the crude (2.17 g) gave 0.25 g **12A** (8.1%), 0.85 g **12B/12A** (55:45, 27.4%), and 1.07 g **12B** (34.5%).

(1S*2R*4S*5R*)-4,8-Dimethyl-5-isopropenyl-8-methoxy-bicyclo[3.3.1]non-7-ene (12A)

Boiling point: 80°C at 0.08 mbar.

¹H-NMR (400MHz, CDCl₃): δ 5.46 (*tq*, $J = 1.4, 3.2$, H-C(7)), 4.64-4.62 (*m*, C=CH₂), 3.33 (*s*, MeO), 3.29 (*dt*, $J = 2.8, 2.9$, H-C(2)), 2.41-2.37 (*br. s*, H-C(1)), 2.11 (*dd*, $J = 3.0, 12.5$, H_{syn}-C(9)), 2.08-2.05 (*m*, C(6)H₂), 1.81 (*ddd*, $J = 3.6, 5.8, 14.6$, H_α-C(3)), 1.74 (*br. quintet*, $J = 7.0$, H-C(4)), 1.69 (*td*, $J = 1.6, 2.1$, MeC(8)), 1.65 (*br. t*, $J = 0.9$, MeC=CH₂),

1.63 (*ddt*, $J = 1.5, 1.8, 15.0$, H_{β} -C(3)), 1.33 (*br. d*, $J = 12.5$, H_{anti} -C(9)), 0.91 (*d*, $J = 7.2$, MeC(4)).

^{13}C -NMR (100MHz, CDCl_3): δ 153.16 (*s*, C(5)C=), 135.24 (*s*, C(8)), 124.13 (*d*, C(7)), 107.26 (*t*, CH_2 =), 77.51 (*d*, C(2)), 56.11 (*q*, MeO), 40.59 (*d*), 39.54 (*t*, C(6)), 39.26 (*s*, C(5)), 36.46 (*d*), 28.29 (*t*, C(9)), 24.85 (*t*, C(3)), 22.34 (*q*, MeC(8)), 18.06 (*q*, MeC=CH₂), 17.92 (*q*, MeC(4)).

MS (EI): 220 (4), 205 (1), 188 (18), 173 (10), 159 (3), 145 (8), 133 (34), 119 (17), 107 (17), 105 (32), 93 (24), 91 (32), 85 (100), 77 (20), 71 (6), 55 (19), 41 (26).

IR: ν_{max} 2962, 2925, 2889, 2826, 1638, 1447, 1375, 1193, 1160, 1118, 1108, 1097, 1081, 970, 959, 924, 886, 829, 804, 786 cm^{-1} .

$[\alpha]_D^{25} = -90.8$ ($c=0.14$, EtOH)

Odour description: woody, ambery

15 (1S*2S*4S*5R*)-4,8-Dimethyl-5-isopropenyl-8-methoxy-bicyclo[3.3.1]non-7-ene (12B)

Boiling point: 80°C at 0.08 mbar.

^1H -NMR (400MHz, CDCl_3): δ 5.55 (*tq*, $J = 1.6, 3.2$, H-C(7)), 4.62 (*quintet*, $J = 1.4$, H_{β} -CH=), 4.57-4.56 (*br. s*, H_{α} -CH=), 3.49 (*dt*, $J = 4.2, 11.6$, H-C(2)), 3.36 (*s*, MeO), 2.66-2.62 (*br. s*, H-C(1)), 2.10-2.00 (*m*, C(6)H₂), 1.95-1.85 (*br. quintet*, $J \approx 7.1$, H-C(4)), 1.81 (*td*, $J = 5.4, 12.2$, H_{α} -C(3)), 1.76 (*dt*, $J = 1.6, 2.2$, MeC(8)), 1.74 (*dd*, $J \approx 2.8, 13.0$, H_{syn} -C(9)), 1.64 (*dd*, $J = 0.5, 1.3$, MeC=CH₂), 1.59 (*ddd*, $J = 1.8, 3.9, 12.8$, H_{anti} -C(9)), 1.56 (*dddd*, $J = 1.4, 2.0, 4.2, 12.6$, H_{β} -C(3)), 0.79 (*d*, $J = 7.2$, MeC(4)).

^{13}C -NMR (100MHz, CDCl_3): δ 152.58 (*s*, C(5)C=), 134.29 (*s*, C(8)), 123.66 (*d*, C(7)), 107.46 (*t*, CH_2 =), 78.58 (*d*, C(2)), 55.98 (*q*, MeO), 40.00 (*t*, C(6)), 39.06 (*s*, C(5)), 38.53 (*d*), 37.11 (*d*), 31.72, 29.58 (2 *t*, C(9), C(3)), 24.42 (*q*, MeC(8)), 18.35 (*q*, MeC=CH₂), 16.43 (*q*, MeC(4)).

MS (EI): 220 (5), 205 (1), 188 (19), 173 (10), 159 (3), 145 (8), 133 (31), 119 (16), 107 (15), 105 (29), 93 (22), 91 (30), 85 (100), 77 (18), 71 (5), 55 (18), 41 (23).

IR: ν_{max} 2965, 2935, 2890, 2828, 1638, 1451, 1374, 1194, 1176, 1103, 1040, 1011, 975, 945, 923, 887, 820, 793, 625 cm^{-1} .

$[\alpha]_D^{25} = -195.4$ ($c=0.76$, EtOH)

Odour description: woody, ambery, fatty, green

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Example 13: A fragrance composition for shower gel

	<u>compound/ingredient</u>	<u>parts by weight 1/1000</u>
5	Armoise oil	5
	Grisalva (5,5,9-Trimethyl-1-ethyltricyclo[8.4.0.0-4,9]-14-oxatetradecane)	5
	Clary sage oil	10
	Jasmonyl (1,3-Nonanediol acetate)	10
	Limette oil	10
10	Patchouli oil	10
	Piconia (Isolongifolanone)	10
	Verbena oil Africa	10
	Oakmoss absolute Tyrol at 50% in DPG	20
	Geranium oil	25
15	Rosemary oil	25
	Sandela (3-Isocamphylcyclohexanol)	25
	Lavandin Grosso oil	30
	Cinnamon leaves oil	30
	Juniper oil	30
20	Methyl cedryl ketone	30
	Dimyrcetol	40
	Fixolide (7-Acetyl-1,1,3,4,4,6-hexamethyltetralin)	40
	Lilial (p-tert-Butyl-alpha-methyldihydrocinnamic aldehyde)	40
	Neroli essential oil	45
25	Bornyl acetate	50
	Cedryl acetate	50
	Para-tert-butylcyclohexyl acetate	50
	Hydroxy citronellal	50
	Irisantheme (alpha-Isomethylionone)	50
30	Linalyl acetate	65
	Galaxolide 50% Benzyl benzoate	65
	Lemon oil Italy	70
	Bergamot oil	90
	5-Isopropenyl-4,8-dimethylbicyclo[3.3.1]non-7-en-2-one (1)	10
35		1000

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Adding 5-Isopropenyl-4,8-dimethylbicyclo[3.3.1]non-7-en-2-one (1) to the fragrance composition adds a sophisticated woody-ambery note with fruity (raspberry) undertones. It also imparts more volume to the woody accord in a fir balsam direction.

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